R E M A R K S

Claims 20 - 37 are pending in the application. Claims 20, 22-25 and 28 - 37 have been amended.

The attached substitute specification is believed to incorporate all the changes requested by the Examiner.

Specifically, the requirements for identification of sequence disclosures has been modified as suggested by the Examiner; the embedded hyperlink has been deleted.

Figure 11 has been properly identified.

Index pages on 37 and 38 have been deleted.

The reference on page 28 has been corrected.

The Examiner's 35 U.S.C. §112, second paragraph objections, have been complied with as far as practical. Applicant's specification does not use the term "hybridize" and the equivalent term "bind" or "bound" as used in applicant's original claims and application has been used. Otherwise, the Examiner's suggestions have been incorporated in toto.

The Examiner's rejection of the claims under 35 U.S.C. §112, first paragraph, as requiring undue experimentation is respectfully traversed. Attached hereto are the declarations as well as their respective CVs under 37 C.F.R. §1.132 of Dr. Richard W. Pastor and James V. Oberthaler.

Both declarations traverse the Examiner's conclusion that undue experimentation is necessary in order to practice the invention. The Oberthaler[1] declaration concludes:

> Finally, in conclusion, I disagree with the Examiner's contention that the trial and error experimentation required to practice the invention amounts to undue experimentation for the following reasons:
>
> (1) As stated earlier, the algorithms presented are straightforward and complete.
>
> (2) No experimentation whatsoever is required. Implementing the algorithms is a routine exercise in program design, coding and debugging. Running them is simply a matter of obtaining the organism-specific genomes and allowing the computer programs to go to work on them.
>
> (3) The only part of the activity that could conceivably be referred to as "experimenting" is the investigation into available bioinformatics resources, such as the syntax and semantics of the resources provided by, for example, that National Library of Medicine's National Center for Biotechnology Information (NCBI). It is clear that in this context, having a ready understanding of this information is a reasonable characteristic of one who could be called "skilled in the art."

Dr. Pastor states as follows:

> The skilled practitioner would turn to the instant description and drawings for guidance in using the claimed invention. The specification provides a detailed roadmap for practicing the invention by one skilled in the art. Referring specifically to the specification and drawings, the introduction at pages 1 - 3 provides a basic description of connectron structure. Figures 1 - 3 are taken from the text by Alberts et al. entitled "The Molecular Biology of the Cell." Pages 3 - 25. Pages 26 - 36 provides a detailed description of a connectron

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[1] Mr. Oberthaler has a minority interest (less than 10%) in a licensee of the invention.

structure. Page 31, the detailed description of the invention, provides a descriptive analysis of the flow diagrams utilized in the computer analysis of connectrons in any given genome. Additionally, ten samples of connectrons found by computer mediation are set out in the specification. Pages 39 - 56 give an example of a prokaryote connectron - E. coli. hence, the algorithm is clearly defined and could be programmed by a skilled scientist. In this sense, the amount of experimentation is quite predictable.

I agree that the nature of the invention, gene control, is complex, and that prior art does not discuss connectron symmetries; i.e., it is my understanding and belief that the connectron invention disclosed in the instant application was made by the inventor, Richard J. Feldmann.

Applicant respectfully submits that, in view of the above-requested amendments to the claims, submission of the substitute specification and the enclosed two declarations under Rule 1.132 traversing the Examiner's undue experimentation rejection, this application is now in condition for allowance, and further and favorable action is respectfully requested.

Respectfully submitted,

Jim Zegeer

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Attachments:
Version With Markings to Show Changes Made
Substitute Specification
Declaration Under 37 C.F.R. §1.132 (Richard W. Pastor)
Declaration Under 37 C.F.R. §1.132 (James V. Oberthaler)

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In the event this paper is deemed not timely filed, the applicant hereby petitions for an appropriate extension of time. The fee for this extension may be charged to Deposit Account No. 26-0090 along with any other additional fees which may be

VERSION WITH MARKINGS TO SHOW CHANGES MADE

Claims 20, 22-25 and 28-37 have been amended as follows:

20. (Amended) A method of identifying DNA sequences that control the expression of different collections of genes in a genome comprising detecting, by computer, one or more pairs of first and second non-adjacent DNA sequences [to which are bound one RNA molecule comprising of two RNA sequences] which could bind to one RNA molecule such that a first RNA sequence in that RNA molecule can bind to a first non-adjacent DNA sequence and a second RNA sequence in that RNA molecule can bind to a second non-adjacent DNA sequence.

22. (Amended) A method of modifying, by computer, the expression of different gene collections in a genome, comprising detecting changes [in connectron behavior that results] in expression of different gene collections in a genome that result in changes in the level of connectron control sequences caused by an exogenous stimulus.

23. (Amended) A method of detecting, by computer, where and when new genes have been integrated into a host genome comprising detecting [the] an operable link between [the] a newly introduced gene and [the] a [existing] preexisting connectron behavior in said host genome.

24. (Amended) A method of detecting, by computer, the expression effect of different gene collections in a given host genome, comprising detecting the [transacting behavior of connectrons between the chromosomes thereof] effect of connectrons on transcription.

25. (Amended) A method of [modifying] changing the expression of different gene collections in a [given] genome comprising

modifying, by a computer, [the] mediated method identification of connectron organization [therein].

28. (Amended) Using the method as defined in claim 20, in prokaryotes, archea, single-celled eukaryotes and multi-celled eukaryotes, where the DNA sequence and the RNA molecule can form a [the] the tetradic relationship such that T1=C1 and T2=C2 where T1 and T2 are DNA sequences 20 or more bases in length, where the C1 sequence is adjacent to the C2 sequence, where the T1 and T2 sequences are on the same chromosome, and where the C1/C2 sequences are on the same chromosome as T1 and T2 or where the C1/C2 sequences are on a chromosome different from T1 and T2, wherein:

C1 sequence - any positive or negative strand DNA sequence of 20 bases or more, the C2 sequence must occur in the same chromosome as the C1 sequence,

C2 sequence - any positive or negative strand DNA sequence of 20 bases or more, the C1 sequence must occur in the same chromosome as the C2 sequence,

C1/C2 - any positive or negative strand DNA sequence of 40 or more bases such that the C1 sequence is adjacent to the C2 sequence,

T1 sequence - any positive or negative strand DNA sequence of 20 bases or more that is on the same chromosome as the T2 sequence, the T1 and T2 sequences must be between about 1kb and 105kb apart, and

T2 sequence - any positive or negative strand DNA sequence of 20 bases or more that is on the same chromosome as the T1

sequence, the T2 or T1 sequences must be between about 1kb and 105kb apart.

29. (Amended) Using the method as defined in claim 20, in prokaryotes, archea, single-celled eukaryotes and multi-celled eukaryotes, where the DNA sequences and the RNA molecule function as a [the] connectron [relationship] that permits many different C1/C2 short loops to control the existence of a T1-T2 long loop and wherein said C1/C2 short lops can be on the same chromosome or on different chromosomes from the T1-T2 long loop, wherein:

C1 sequence - any positive or negative strand DNA sequence of 20 bases or more, the C2 sequence must occur in the same chromosome as the C1 sequence,

C2 sequence - any positive or negative strand DNA sequence of 20 bases or more, the C1 sequence must occur in the same chromosome as the C2 sequence,

C1/C2 - any positive or negative strand DNA sequence of 540 or more bases such that the C1 sequence is adjacent to the C2 sequence,

T1 sequence - any positive or negative strand DNA sequence of 20 bases or more that is on the same chromosome as the T2 sequence, the T1 and T2 sequences must be between about 1kb and 105kb apart, and

T2 sequence - any positive or negative strand DNA sequence of 20 bases or more that is on the same chromosome as the T1 sequence, the T2 or T1 sequences must be between about 1kb and 105kb apart.

30. (Amended) Using the method as defined in claim 20, in prokaryotes, archea, single-celled eukaryotes and multi-celled eukaryotes, where the DNA sequences and the RNA molecule function as a [the] connectron [relationship] that permits one C1/C2 short loop to control the existence of many T1-T2 long loops, the C1/C2 short loop can be on the same chromosome or on different chromosomes from the T1-T2 long loops, wherein:

C1 sequence - any positive or negative strand DNA sequence of 20 bases or more, the C2 sequence must occur in the same chromosome as the C1 sequence,

C2 sequence - any positive or negative strand DNA sequence of 20 bases or more, the C1 sequence must occur in the same chromosome as the C2 sequence,

C1/C2 - any positive or negative strand DNA sequence of 40 or more bases such that the C1 sequence is adjacent to the C2 sequence,

T1 sequence - any positive or negative strand DNA sequence of 20 bases or more that is on the same chromosome as the T2 sequence, the T1 and T2 sequences must be between about 1kb and 105kb apart, and

T2 sequence - any positive or negative strand DNA sequence of 20 bases or more that is on the same chromosome as the T1 sequence, the T2 or T1 sequences must be between about 1kb and 105kb apart.

31. (Amended) Using the method as defined in claim 20, where the DNA sequences and the RNA molecule function as a [the] connectron [relationships] between prokaryotes and their plasmids and wherein

said [connectrons implement] connectron implements a control mechanism between the two genomes that makes it possible from them to form a symbiotic relationship, and in the case of D. radiodurans the relationship is not symmetric, and the D. radiodurans genome sends C1/C2 short loops to the MP1 plasmid, wherein:

C1 sequence - any positive or negative strand DNA sequence of 20 bases or more, the C2 sequence must occur in the same chromosome as the C1 sequence,

C2 sequence - any positive or negative strand DNA sequence of 20 bases or more, the C1 sequence must occur in the same chromosome as the C2 sequence,

C1/C2 - any positive or negative strand DNA sequence of 40 or more bases such that the C1 sequence is adjacent to the C2 sequence,

T1 sequence - any positive or negative strand DNA sequence of 20 bases or more that is on the same chromosome as the T2 sequence, the T1 and T2 sequences must be between about 1kb and 105kb apart, and

T2 sequence - any positive or negative strand DNA sequence of 20 bases or more that is on the same chromosome as the T1 sequence, the T2 or T1 sequences must be between about 1kb and 105kb apart.

32. (Amended) Using the method as defined in claim 20, where the DNA sequences and the RNA molecule function as a [the] connectron [relationships] that exist in a plant or a higher [animals] animal.

33. (Amended) Using the method as defined in claim 20, in prokaryotes, archea, single-celled eukaryotes and multi-celled eukaryotes, [the] where the DNA sequences and the RNA molecule function as a connectron [relationship] that permits one C1/C2 short loop to control the existence of one or more T1-T2 long loops without being subject to any expression controls other than those of the gene to which the C1/C2 is 3'UTR, wherein:

C1 sequence - any positive or negative strand DNA sequence of 20 bases or more, the C2 sequence must occur in the same chromosome as the C1 sequence,

C2 sequence - any positive or negative strand DNA sequence of 20 bases or more, the C1 sequence must occur in the same chromosome as the C2 sequence,

C1/C2 - any positive or negative strand DNA sequence of 40 or more bases such that the C1 sequence is adjacent to the C2 sequence,

T1 sequence - any positive or negative strand DNA sequence of 20 bases or more that is on the same chromosome as the T2 sequence, the T1 and T2 sequences must be between about 1kb and 105kb apart,

T2 sequence - any positive or negative strand DNA sequence of 20 bases or more that is on the same chromosome as the T1 sequence, the T2 or T1 sequences must be between about 1kb and 105kb apart, and

3'UTR - untranslated 3' end of an mRNA is beyond the end of the last exon, a stop codon in the mRNA causes the ribosome to stop the translation of mRNA into protein.

34. (Amended) Using the method as defined in claim 20, in prokaryotes, archea, single-celled eukaryotes and multi-celled eukaryotes, [the] where the DNA sequences and the RNA molecule function as a connectron [relationship] that permits one C1/C2 short loop to control the existence of one or more T1-T2 long loops such that this C1/C2 short loop is itself subject to expression control by another T1-T2 long loop which surrounds it, wherein:

C1 sequence - any positive or negative strand DNA sequence of 20 bases or more, the C2 sequence must occur in the same chromosome as the C1 sequence,

C2 sequence - any positive or negative strand DNA sequence of 20 bases or more, the C1 sequence must occur in the same chromosome as the C2 sequence,

C1/C2 - any positive or negative strand DNA sequence of 40 or more bases such that the C1 sequence is adjacent to the C2 sequence,

T1 sequence - any positive or negative strand DNA sequence of 20 bases or more that is on the same chromosome as the T2 sequence, the T1 and T2 sequences must be between about 1kb and 105kb apart, and

T2 sequence - any positive or negative strand DNA sequence of 20 bases or more that is on the same chromosome as the T1 sequence, the T2 or T1 sequences must be between about 1kb and 105kb apart.

35. (Amended) Using the method as defined in claim 20, in prokaryotes, archea, single-celled eukaryotes and multi-celled eukaryotes, [the] where the DNA sequences and the RNA molecule

function as a connectron [relationship] that permits one C1/C2 short loop to control the existence of the T1-T2 long loop that surrounds it, wherein:

C1 sequence - any positive or negative strand DNA sequence of 20 bases or more, the C2 sequence must occur in the same chromosome as the C1 sequence,

C2 sequence - any positive or negative strand DNA sequence of 20 bases or more, the C1 sequence must occur in the same chromosome as the C2 sequence,

C1/C2 - any positive or negative strand DNA sequence of 50 or more bases such that the C1 sequence is adjacent to the C2 sequence,

T1 sequence - any positive or negative strand DNA sequence of 20bases or more that is on the same chromosome as the T2 sequence, the T1 and T2 sequences must be between about 1kb and 105kb apart, and

T2 sequence - any positive or negative strand DNA sequence of 20 bases or more that is on the same chromosome as the T1 sequence, the T2 or T1 sequences must be between about 1kb and 105kb apart.

36. (Amended) Using the method as defined in claim 20, [the connectron relationship] where the DNA sequences and the RNA molecule function as a connectron that do not have any genes within the T1-T2 long loop, wherein:

T1 sequence is any positive or negative strand DNA sequence of 20 bases or more that is on the same chromosome as the T2 sequence, and

T2 sequence - any positive or negative strand DNA sequence of 20 bases or more that is on the same chromosome as the T1 sequence, and the T2 or T1 sequences must be between about 1kb and 105kb apart.

37. (Amended) Using the method as defined in claim 20, <u>where the DNA sequences and the RNA molecule function as a</u> [the] geneless connectron [relationship] where one C1/C2 short loop controls the existence of many geneless T1-T2 long loops, wherein:

C1 sequence - any positive or negative strand DNA sequence of 20 bases or more, the C2 sequence must occur in the same chromosome as the C1 sequence,

C2 sequence - any positive or negative strand DNA sequence of 20 bases or more, the C1 sequence must occur in the same chromosome as the C2 sequence,

C1/C2 - any positive or negative strand DNA sequence of 40 or more bases such that the C1 sequence is adjacent to the C2 sequence,

T1 sequence - any positive or negative strand DNA sequence of 20 bases or more that is on the same chromosome as the T2 sequence, the T1 and T2 sequences must be between about 1kb and 105kb apart, and

T2 sequence - any positive or negative strand DNA sequence of 20 bases or more that is on the same chromosome as the T1

sequence, the T2 or T1 sequences must be between about 1kb and 105kb apart.